

Atty Dkt. No.: STAN131
USSN: 09/716,842

AMENDMENTS

In the claims:

Claims 1-15 (Cancelled).

16. **(Currently Amended)** A method for directing the biodistribution of a drug that binds to a protein target, wherein the drug is directed to an intracellular space upon administration to a mammalian host, said method comprising:

administering to said mammalian host an effective amount of a bifunctional molecule having a molecular weight that does not exceed about 5000 daltons consisting of a drug moiety comprising said drug or an active derivative thereof and a targeting moiety to an intracellular biodistribution modulating protein optionally joined by a linking group, wherein said drug moiety binds to a protein target and said targeting moiety has an affinity for its intracellular biodistribution modulating protein of at least about 10^{-4} M, and wherein said bifunctional molecule has a modulated biodistribution upon administration to said mammalian host as compared to a free drug control;

to direct said biodistribution of said drug upon administration to said host to an intracellular space as compared to a free drug control.

17. **(Currently Amended)** The method according to Claim 16, wherein said bifunctional molecule exhibits enhanced efficacy upon administration to said mammalian host as compared to a free drug control.

18. **(Currently Amended)** The method according to Claim 16, wherein said bifunctional molecule exhibits reduced toxicity upon administration to said mammalian host as compared to a free drug control.

Claims 19 - 21. (Cancelled)

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22. **(Previously Presented)** The method according to Claim 16, wherein said bifunctional molecule comprises a linking group.

23. **(Previously Presented)** The method according to Claim 16, wherein said bifunctional molecule is administered as a pharmaceutical preparation.

24. **(Currently Amended)** A method for targeting a drug to an intracellular site of a mammalian host, said method comprising:

administering to said mammalian host an effective amount of a bifunctional molecule comprising consisting of a drug moiety and a targeting moiety optionally joined by a linking group, wherein said drug moiety and targeting moiety moieties bind to intracellular proteins and said targeting moiety has an affinity for its intracellular protein of at least about 10^{-4} M, and wherein said bifunctional molecule exhibits a modulated biodistribution upon administration to a mammalian host as compared to a free drug control;

to target said drug to an intracellular site of a mammalian host.

25. **(Original)** The method according to Claim 24, wherein said bifunctional molecule comprises a linking group.

26. **(Original)** The method according to Claim 24, wherein said bifunctional molecule does not include a linking group.

Claims 27-29. (Canceled)

30. **(Currently Amended)** In a method of administering a drug to a host in need of said drug, the improvement comprising:

administering to said host an effective amount of a bifunctional molecule having a molecular weight that does not exceed about 5000 daltons and consisting of said drug

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moiety comprising said drug or a derivative thereof covalently linked, either directly or through an optional linking group, to a targeting moiety that binds to an intracellular biodistribution modulating protein, wherein said drug moiety binds to an intracellular protein and said targeting moiety has an affinity for its intracellular biodistribution modulating protein of at least about 10^{-4} M.

31. (Previously Presented) The method according to Claim 30, wherein said host is a mammalian host.

32. (Previously Presented) The method according to Claim 31, wherein said mammalian host is human.

33. (Original) The method according to Claim 30, wherein said drug is a small molecule.

34. (Original) The method according to Claim 30, wherein said targeting moiety binds to an endogenous biodistribution modulating protein.

Claim 35. (Cancelled)

36. (Original) The method according to Claim 34, wherein said endogenous biodistribution modulating protein is an intracellular protein.

Claims 37-38 (Cancelled)

39. (Previously Presented) The method according to Claim 16, wherein said targeting moiety is a peptidyl-prolyl isomerase ligand.

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40. **(Previously Presented)** The method according to Claim 39, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP or cyclophilin.

41. **(Previously Presented)** The method according to Claim 40, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP.

42. **(Previously Presented)** The method according to Claim 41, wherein said peptidyl-prolyl isomerase ligand is selected from the group consisting of FK506 and rapamycin.

43. **(Previously Presented)** The method according to Claim 39, wherein said peptidyl-prolyl isomerase ligand is a ligand for a cyclophilin.

44. **(Previously Presented)** The method according to Claim 43, wherein said peptidyl-prolyl isomerase ligand is a cyclosporin.

45. **(Previously Presented)** The method according to Claim 24, wherein said targeting moiety is a peptidyl-prolyl isomerase ligand.

46. **(Previously Presented)** The method according to Claim 45, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP or cyclophilin.

47. **(Previously Presented)** The method according to Claim 46, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP.

48. **(Previously Presented)** The method according to Claim 47, wherein said peptidyl-prolyl isomerase ligand is selected from the group consisting of FK506 and rapamycin.

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49. **(Previously Presented)** The method according to Claim 46, wherein said peptidyl-prolyl isomerase ligand is a ligand for a cyclophilin.

50. **(Previously Presented)** The method according to Claim 49, wherein said peptidyl-prolyl isomerase ligand is a cyclosporin.

51. **(Previously Presented)** The method according to Claim 30, wherein said targeting moiety is a peptidyl-prolyl isomerase ligand.

52. **(Previously Presented)** The method according to Claim 51, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP or cyclophilin.

53. **(Previously Presented)** The method according to Claim 52, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP.

54. **(Previously Presented)** The method according to Claim 53, wherein said peptidyl-prolyl isomerase ligand is selected from the group consisting of FK506 and rapamycin.

55. **(Previously Presented)** The method according to Claim 53, wherein said peptidyl-prolyl isomerase ligand is a ligand for a cyclophilin.

56. **(Previously Presented)** The method according to Claim 55, wherein said peptidyl-prolyl isomerase ligand is a cyclosporin.